CLAIMS

WHAT IS CLAIMED IS:

1. An isolated nucleic acid molecule comprising a nucleotide sequence selected from the group consisting of:

(a) the nucleotide sequence as set forth in SEQ ID NOS: 1 or 3;

(b) a nucleotide sequence encoding the polypeptide set forth in SEQ ID NOS: 2 or 4;

(c) a nucleotide sequence which hybridizes under moderately or highly stringent conditions to the complement of (a) or (b); and

(e) a nucleotide sequence complementary to any of (a)-(c).

2. An isolated nucleic acid molecule comprising a nucleotide sequence selected from the group consisting of:

(a) a nucleotide sequence encoding a polypeptide that is at least about 70, 75, 80, 85, 90, 95, 96, 97, 98, or 99 percent identical to the polypeptide set forth in SEQ ID NOS: 2 or 4, wherein the encoded polypeptide has an activity of the polypeptide set forth in SEQ ID NOS: 2 or 4;

(b) a nucleotide sequence encoding an allelic variant or splice variant of the nucleotide sequence as set forth in SEQ ID NOS: 1 or 3;

(c) a nucleotide sequence of SEQ ID NOS: 1; 3; (a); or (b) encoding a polypeptide fragment of at least about 25 amino acid residues, wherein the polypeptide has an activity of the polypeptide set forth in SEQ ID NOS: 2 or 4;

(d) a nucleotide sequence of SEQ ID NOS: 1, 3, or (a)-(c) comprising a fragment of at least about 16 nucleotides;

(e) a nucleotide sequence which hybridizes under moderately or highly stringent conditions to the complement of any of (a)-(d); and

(f) a nucleotide sequence complementary to any of (a)-(c).

3. An isolated nucleic acid molecule comprising a nucleotide sequence selected from the group consisting of:

(a) a nucleotide sequence encoding a polypeptide set forth in SEQ ID NOS: 2 or 4 with at least one conservative amino acid substitution, wherein the polypeptide has an activity of the polypeptide set forth in SEQ ID NOS: 2 or 4;

(b) a nucleotide sequence encoding a polypeptide set forth in SEQ ID NOS: 2 or 4 with at least one amino acid insertion, wherein the polypeptide has an activity of the polypeptide set forth in SEQ ID NOS: 2 or 4;

(c) a nucleotide sequence encoding a polypeptide set forth in SEQ ID NOS: 2 or 4 with at least one amino acid deletion, wherein the polypeptide has an activity of the polypeptide set forth in SEQ ID NOS: 2 or 4;

(d) a nucleotide sequence encoding a polypeptide set forth in SEQ ID NOS: 2 or 4 which has a C- and/or N- terminal truncation, wherein the polypeptide has an activity of the polypeptide set forth in SEQ ID NOS: 2 or 4;

(e) a nucleotide sequence encoding a polypeptide set forth in SEQ ID NOS: 2 or 4 with at least one modification selected from the group consisting of amino acid substitutions, amino acid insertions, amino acid deletions, C-terminal truncation, and N-terminal truncation, wherein the polypeptide has an activity of the polypeptide set forth in SEQ ID NOS: 2 or 4;

(f) a nucleotide sequence of (a)-(e) comprising a fragment of at least about 16 nucleotides;

(g) a nucleotide sequence which hybridizes under moderately or highly stringent conditions to the complement of any of (a)-(f); and

(h) a nucleotide sequence complementary to any of (a)-(e).

4. A vector comprising the nucleic acid molecule of claims 1, 2, or 3.

5. A host cell comprising the vector of claim 4.

6. The host cell of claim 5 that is a eukaryotic cell.

7. The host cell of claim 5 that is a prokaryotic cell.

8. A process of producing a huE3α polypeptide comprising culturing the host cell of claim 5 under suitable conditions to express the polypeptide, and optionally isolating the polypeptide from the culture.

9. A polypeptide produced by the process of claim 8.

10. The process of claim 8, wherein the nucleic acid molecule comprises promoter DNA other than the promoter DNA for the native huE3α polypeptide operatively linked to the DNA encoding the huE3α polypeptide.

11. The isolated nucleic acid molecule according to claim 2 wherein the percent identity is determined using a computer program selected from the group consisting of GAP, BLASTP, BLASTN, FASTA, BLASTA, BLASTX, BestFit, and the Smith-Waterman algorithm.

12. A process for determining whether a compound inhibits huE3α polypeptide activity or production comprising exposing a cell according to claims 5, 6, or 7 to the compound, and measuring huE3α polypeptide activity or production in said cell.

13. An isolated polypeptide comprising the amino acid sequence set forth in SEQ ID NOS: 2 or 4.

14. An isolated polypeptide comprising the amino acid sequence selected from the group consisting of:

(a) the mature amino acid sequence as set forth in SEQ ID NOS: 2 or 4 comprising a mature amino terminus at residue 1, optionally further comprising an amino-terminal methionine;

(b) an amino acid sequence for an ortholog of SEQ ID NOS: 2 or 4;

(c) an amino acid sequence that is at least about 70, 80, 85, 90, 95, 96, 97, 98, or 99 percent identical to the amino acid sequence of SEQ ID NOS: 2 or 4, wherein the polypeptide has an activity of the polypeptide set forth in SEQ ID NOS: 2 or 4;

(d) a fragment of the amino acid sequence set forth in SEQ ID NOS: 2 or 4 comprising at least about 25 amino acid residues, wherein the polypeptide has an activity of the polypeptide set forth in SEQ ID NOS: 2 or 4;

(e) an amino acid sequence for an allelic variant or splice variant of either the amino acid sequence as set forth in SEQ ID NOS: 2 or 4, or at least one of (a)-(c).

15. An isolated polypeptide of claim 14 wherein the amino acid sequence is a mouse ortholog set out in SEQ ID NO: 6.

16. An isolated polypeptide comprising the amino acid sequence selected from the group consisting of:

(a) the amino acid sequence as set forth in SEQ ID NOS: 2 or 4 with at least one conservative amino acid substitution, wherein the polypeptide has an activity of the polypeptide set forth in SEQ ID NOS: 2 or 4;

(b) the amino acid sequence as set forth in SEQ ID NOS: 2 or 4 with at least one amino acid insertion, wherein the polypeptide has an activity of the polypeptide set forth in SEQ ID NOS: 2 or 4;

(c) the amino acid sequence as set forth in SEQ ID NOS: 2 or 4 with at least one amino acid deletion, wherein the polypeptide has an activity of the polypeptide set forth in SEQ ID NOS: 2 or 4;

(d) the amino acid sequence as set forth in SEQ ID NOS: 2 or 4 which has a C- and/or N- terminal truncation, wherein the polypeptide has an activity of the polypeptide set forth in SEQ ID NOS: 2 or 4; and

(e) the amino acid sequence as set forth in SEQ ID NOS: 2 or 4, with at least one modification selected from the group consisting of amino acid substitutions, amino acid insertions, amino acid deletions, C-terminal truncation, and N-terminal truncation, wherein the polypeptide has an activity of the polypeptide set forth in SEQ ID NOS: 2 or 4.

17. An isolated polypeptide encoded by the nucleic acid molecule of claims 1, 2, or 3.

18. The isolated polypeptide according to claim 14 wherein the percent identity is determined using a computer program selected from the group consisting of GAP, BLASTP, BLASTN, FASTA, BLASTA, BLASTX, BestFit, and the Smith-Waterman algorithm.

19. An antibody produced by immunizing an animal with a peptide comprising an amino acid sequence of SEQ ID NOS: 2 or 4.

20. An antibody or fragment thereof that specifically binds the polypeptide of claims 13, 14, 15 or 16.

21. The antibody of claim 20 that is a monoclonal antibody.

22. A hybridoma that produces a monoclonal antibody that binds to a peptide comprising an amino acid sequence of SEQ ID NOS: 2 or 4.

23. A method of detecting or quantitating the amount of huE3α polypeptide using the anti-huE3α antibody or fragment of claims 18, 19, or 20.

24. A method for determining the presence and/or concentration of huE3α polypeptide in a biological sample comprising the steps of:

(a) obtaining a biological sample;

(b) contacting the biological sample with an antibody according to claim 22 under conditions which allow for the antibody to bind to the huE3α polypeptide;

(c) detecting antibody binding to huE3α polypeptide in the biological sample, wherein the detection of antibody binding is indicative of the presence of huE3α polypeptide in said biological sample; and

(d) comparing the level of antibody binding to huE3α polypeptide within said biological sample and the level of the antibody binding to a known concentration of huE3α polypeptide.

25. A selective binding agent or fragment thereof that specifically binds at least one polypeptide wherein said polypeptide comprises the amino acid sequence selected from the group consisting of:

(a) the amino acid sequence as set forth in SEQ ID NOS: 2 or 4; and

(b) fragment of the amino acid sequence set forth in at least one of SEQ ID NOS: 2 or 4; or a naturally occurring variant thereof.

26. The selective binding agent of claim 25 that is an antibody or fragment thereof.

27. The selective binding agent of claim 25 that is a humanized antibody.

28. The selective binding agent of claim 25 that is a human antibody or fragment thereof.

29. The selective binding agent of claim 25 that is a polyclonal antibody or fragment thereof.

30. The selective binding agent claim 25 that is a monoclonal antibody or fragment thereof.

31. The selective binding agent of claim 25 that is a chimeric antibody or fragment thereof.

32. The selective binding agent of claim 25 that is a CDR-grafted antibody or fragment thereof.

33. The selective binding agent of claim 25 that is an antiidiotypic antibody or fragment thereof.

34. The selective binding agent of claim 25 which is a variable region fragment.

35. The variable region fragment of claim 25 which is a Fab or a Fab' fragment.

36. A selective binding agent or fragment thereof comprising at least one complementarity determining region with specificity for a polypeptide having the amino acid sequence of SEQ ID NOS: 2 or 4.

37. The selective binding agent of claim 25 which is bound to a detectable label.

38. A selective binding agent produced by immunizing an animal with a polypeptide comprising an amino acid sequence selected from the group consisting of SEQ ID NOS: 2 or 4.

39. A hybridoma that produces a selective binding agent capable of binding a polypeptide according to claims 1, 2, or 3.

40. A composition comprising the polypeptide of claims 13, 14, or 16 and a pharmaceutically acceptable formulation agent.

41. The composition of claim 40 wherein the pharmaceutically acceptable formulation agent is a carrier, adjuvant, solubilizer, stabilizer, or anti-oxidant.

42. The composition of claim 40 wherein the polypeptide comprises the mature amino acid sequence as set forth in SEQ ID NOS: 2 or 4.

43. A polypeptide comprising a derivative of the polypeptide of claims 13, 14, or 16.

44. The polypeptide of claim 43 which is covalently modified with a water-soluble polymer.

45. The polypeptide of claim 44 wherein the water-soluble polymer is selected from the group consisting of polyethylene glycol, monomethoxy-polyethylene glycol, dextran, cellulose, poly-(N-vinyl pyrrolidone) polyethylene glycol, propylene glycol homopolymers, polypropylene oxide/ethylene oxide co-polymers, polyoxyethylated polyols, and polyvinyl alcohol.

46. A composition comprising a nucleic acid molecule of claims 1, 2, or 3 and a pharmaceutically acceptable formulation agent.

47. A composition of claim 46 wherein said nucleic acid molecule is contained in a viral vector.

48. A viral vector comprising a nucleic acid molecule of claims 1, 2, or 3.

49. A fusion polypeptide comprising the polypeptide of claims 13, 14, or 16 fused to a heterologous amino acid sequence.

50. The fusion polypeptide of claim 49 wherein the heterologous amino acid sequence is an IgG constant domain or fragment thereof.

51. A method for treating, preventing or ameliorating a medical condition in a mammal resulting from decreased levels of huE3α polypeptide comprising administering a huE3α polypeptide to said mammal.

52. The method of claim 51 wherein the huE3α polypeptide administered is the amino acid sequence set forth in SEQ ID NOS: 2 or 4 or a fragment thereof at least 25 amino acids or a homolog, analog or variant of said huE3α polypeptide or fragment thereof.

53. The method of claim 51 wherein the huE3α polypeptide administered has the amino acid set forth in SEQ ID NOS: 2 or 4 with at least one amino acid substitution.

54. The method of claim 51 wherein the huE3α polypeptide administered has the amino acid sequence set forth in SEQ ID NOS: 2 or 4 with at least one amino acid deleted.

55. A method of diagnosing the existence or a susceptibility to a pathological condition in a subject caused by or resulting from abnormal levels of huE3α in a mammalian subject comprising:

(a) determining the level of huE3α in a biological, tissue or cellular sample; and

(b) comparing the level of huE3α polypeptide in biological, tissue or cellular samples form normal subjects or the subject at an earlier time; wherein a susceptibility of an existence of a pathological condition is based on the presence or amount of expression of huE3α polypeptide.

56. A device, comprising:

(a) a membrane suitable for implantation; and

(b) cells encapsulated within said membrane, wherein said cells secrete a protein of claims 13, 14, or 16; said membrane being permeable to said protein product and impermeable to materials detrimental to said cells.

57. A device, comprising:

(a) a membrane suitable for implantation; and

(b) The huE3α polypeptide encapsulated within said membrane, wherein said membrane is permeable to the polypeptide.

58. A method of identifying a compound which binds to a polypeptide comprising:

(a) contacting the polypeptide of claims 13, 14, or 16 with a compound; and

(b) determining the extent of binding of the polypeptide to the compound.

59. A diagnostic reagent comprising a detectably labeled polynucleotide encoding the amino acid sequence set out in SEQ ID NOS: 2 or 4; or a fragment, variant or homolog thereof including allelic variants and spliced variants thereof.

60. The diagnostic reagent of claim 58, wherein said labeled polynucleotide is a first-strand cDNA.

61. A method for determine the presence of huE3α nucleic acids in a biological sample comprising the steps of:

(a) providing a biological sample suspected of containing huE3α nucleic acids;

(b) contacting the biological sample with a diagnostic reagent according to claim 59 under conditions wherein the diagnostic reagent will hybridize with huE3α nucleic acids contained in said biological sample;

(c) detecting hybridization between huE3α nucleic acid in the biological sample and the diagnostic reagent; and

(d) comparing the level of hybridization between the biological sample and diagnostic reagent with the level of hybridization between a known concentration of huE3α nucleic acid and the diagnostic reagent.

62. A method for detecting the presence of huE3α nucleic acids in a tissue or cellular sample comprising the steps of:

(a) providing a tissue or cellular sample suspected of containing huE3α nucleic acids;

(b) contacting the tissue or cellular sample with a diagnostic reagent according to claim 59 under conditions wherein the diagnostic reagent will hybridize with huE3α nucleic acids;

(c) detecting hybridization between huE3α nucleic acid in the tissue or cellular sample and the diagnostic reagent; and

(d) comparing the level of hybridization between the tissue or cellular sample and diagnostic reagent with the level of hybridization between a known concentration of huE3α nucleic acid and the diagnostic reagent.

63. The method of claim 59 wherein said polynucleotide molecule is DNA.

64. The method of claim 59 wherein said polynucleotide molecule is RNA.

65. A method of modulating levels of a polypeptide in an animal comprising administering to the animal the nucleic acid molecule of claims 1, 2, or 3.

66. A transgenic non-human mammal comprising the nucleic acid molecule of claims 1, 2, or 3.